

**Working Title:** Analysis of male reproductive effects related to the phthalate syndrome

**Authors:** Todd Blessinger<sup>1\*</sup>, Susan Y. Euling<sup>1</sup>, Anne-Marie Saillenfait<sup>2</sup>, Lily Wang<sup>3</sup>, Karen Hogan<sup>1</sup>, Christine Cai<sup>1</sup>

1. US EPA National Center for Environmental Assessment, Washington, DC
2. Institut National de Recherche et de Sécurité (INRS), Vandoeuvre, France
3. US EPA National Center for Environmental Assessment, Research Triangle Park, NC

\*Corresponding author; [ [HYPERLINK "mailto:Blessinger.Todd@epa.gov"](mailto:Blessinger.Todd@epa.gov) ]

**Abstract:**

Gestational exposure of male rats to certain phthalates results in a phenotype known as “phthalate syndrome”, which is characterized by effects including cryptorchidism, reduced anogenital distance, female-like nipple retention, hypospadias, and other reproductive tract malformations. As these endpoints are functionally related to one another, the National Research Council (2008) recommends an approach where an animal is designated as having phthalate syndrome if it exhibits at least one of these endpoints. The purpose of this publication is to evaluate the interrelationships among the endpoints that characterize phthalate syndrome, using data from a gestational exposure study in Sprague-Dawley rats by Saillenfait et al. 2008. Specifically, Saillenfait et al. (2008) exposed dams to one of five doses of diisobutyl phthalate (DIBP) or vehicle control from gestation day 12-21, and assessed both continuous and dichotomous endpoints of reproductive development in male offspring. Using that dataset, this publication will evaluate whether some endpoints were more sensitive to DIBP exposure (more frequent, observed at lower doses) and whether some endpoints occur consistently together. A multivariate analysis on the dichotomous phthalate syndrome endpoint data will be conducted to determine the relationships based on correlations, principal components, and other metrics. These relationships may provide predictions for these endpoints for other data sets and other phthalate esters. *(The views expressed are those of the authors and do not necessarily represent the views or policies of the US EPA.)*

**References:**

Saillenfait AM, Sabaté JP, Gallissot F. Diisobutyl phthalate impairs the androgen-dependent reproductive development of the male rat. *Reprod Toxicol.* 2008 Oct, 26(2): 107-15

National Research Council (NRC). Phthalate and cumulative risk assessment: The tasks ahead. Committee on the Health Risks of Phthalates, Board on Environmental Studies and Toxicology, Division on Earth and Life Sciences. The National Academies Press, Washington, DC, 2008